Remarks

Claims 1-12 were pending. Due to the restriction requirement, claims 4-9 and 11-12 are withdrawn due to the restriction requirement. No claims are added. Therefore, claims 1-3 and 10 are under consideration.

The support for the amendment to claim 1 can be found on page 35, lines 8-9 and FIG. 12B of the specification. Claim 3 is amended to correct typographical errors.

No new matter is introduced by this amendment.

Claim objection

Claim 3 is objected to due to the taxonomy language. Claim 3 is amended to recite the genus names of the viruses as suggested by the Examiner. In view of this amendment, Applicants request that he objection to claim 3 be withdrawn.

35 U.S.C. § 102/103

Claims 1-3 and 10 are rejected under 35 U.S.C. § 102(b) as anticipated by, or in the alternative under § 103 as unpatentable, in view of Kim *et al.* (*Mol. Cells* 30:165-9, 1997). Applicants disagree and request reconsideration.

The claimed virus suppressing actor (VSF) protein is different from the virus inhibitor substance (VIS) disclosed in the Kim *et al.* document. The VIS recited in Kim *et al.* is culture supernatant, not an isolated polypeptide (see lines 5-9, right column, page 166 of Kim *et al.*). Culture supernatant is heterogeneous and undefined composition. Thus, the isolated VSF protein of the present invention is not anticipated or unpatentable in view of the Kim *et al.* reference.

In addition, the VIS recited in Kim *et al.* and the VSF protein of the present invention originated from different sources. The VIS is originated from hybridoma 12D8. On the other hand, the VSF protein originated from hybridoma 4D1B prepared using a mouse intraperiotoneally injected with EMC-DV. Thus, the isolated VSF protein of the present invention is not anticipated or unpatentable in view of the Kim *et al.* reference.

The physio-biochemical properties of both materials are different. For example, the heat stability of the VIS of Kim *et al.* at 56°C is very poor (See Table 2 of Kim *et al.*), while the VSF

of the present invention is highly stable at 56°C up to 50 minutes (See Fig. 12B and Example 19 on page 35 of the specification). Claim 1 is amended to further clarify that the VSF of the present invention is heat stable at 56°C for about 40 minutes. This is different from the VIS of Kim *et al.* which is not stable at 56°C.

In addition, mice periotoneally injected with EMC-D and the VSF protein of the present invention after 24 hrs from the viral infection showed resistance against diabetes completely (See Example 13 and Table 5 of the specification), while 67% of mice periotoneally injected with EMC-D and the VIS of Kim *et al.,* even after 4 hrs from the viral infection, suffered from diabetes (See Table 1 of Kim *et al.*). This further demonstrates that the VIS of Kim *et al.* is different from the VSF of the present invention.

Because the claimed VSF protein is different from the VIS disclosed in the Kim *et al.* reference, and the VIS disclosed in the Kim *et al.* does not render the claimed VSF unpatentable, Applicants request that the rejection under 35 U.S.C. § 102/103 be withdrawn.

35 U.S.C. § 112 first paragraph

Claims 1, 3, and 10 are rejected under 35 U.S.C. § 112 first paragraph, as failing to comply with the enablement requirement. Applicants disagree and request reconsideration.

The elected claims are directed to an isolated virus suppressing factor (VSF) protein. The elected claims are not directed to methods of treating viral infections. Therefore, rejecting the composition claims as lacking enablement is not appropriate. In any event, the claims are sufficiently enabled.

In regard to the scope of the claims, the specification provides a significant number of examples demonstrating the antiviral activity of virus suppressing factor (VSF). The specification teaches that VSF inhibits viral infection or replication of six different viruses from five virus families: *Picornaviridae* (EMCV and Mengo virus, See Example 10 starting on page 27 of the specification and Example 13 starting on page 30 of the specification), *Orthomyxoviridae* (influenza virus, See Example 11 starting on page 28 of the specification), *Retroviridae* (HIV, See Example 12 starting on page 29 of the specification), *Herpesviridae* (HCMV, See Example 14 on page 32 of the specification) and *Rhabdoviridae* (vesicular stomatitis virus, See Example 23 on page 37 of the specification). In addition, as shown in Exhibit A, VSF has antiviral activity against Coxsackie B4 virus (*Picornaviridae* family), as

detected with a modified virus inhibition test (MVIT). [If the examiner would prefer that Exhibit A be presented in a Rule 132 Declaration, Applicants are willing to do so.] Given the breadth of examples provided in the specification, undue experimentation would not be required of one of skill in the art to use the claimed VSF proteins.

On pages 5-6 of the Office action, a number of publications are cited to indicate that vaccines against the claimed virus families have not yet been developed, and thus undue experimentation is required to develop a vaccine capable of preventing or treating viral infections as claimed. However, this point is not relevant. The claimed VSF proteins are not vaccines, therefore, the cited references have no bearing. The claimed VSF proteins have antiviral activity. In addition, it is noted on page 6 of the Office action that since effective vaccines have not been developed, other types of drugs are being used. This conclusion supports the use of VSF, which is a compound that is shown in the specification to possess antiviral activity.

It is also asserted on page 6 of the Office action that the working examples focus on *in vitro* or *in ovo* studies. However, it is not always necessary to provide *in vivo* working examples, particularly for the full scope of the claims. Although the current application primarily uses *in vitro* systems to test VSF, the study described in Example 13 demonstrates that VSF is effective *in vivo* at preventing the development of diabetes mellitus in mice infected with EMCV. This data correlates with the *in vitro* antiviral activity observed with VSF in cells infected with EMCV (Example 10). Additional *in vivo* data is provided in Example 11 for the influenza virus (methods used embryonated chicken eggs). Since the specification provides (i) *in vitro* data for a number of viruses, (ii) *in vivo* data for two viruses and (iii) correlates the *in vitro* antiviral activity of VSF with the *in vivo* activity, the claims are fully enabled for both *in vitro* and *in vivo* use.

It is asserted on page 6 of the Office action that the ability of VSF to inhibit activity of viruses other than EMC-DV is questionable because VSF possesses properties similar to antibodies and would thus specifically interact with EMC-DV. Applicants disagree and request reconsideration. Although VSF does share some sequence similarities with particular peptides of an immunoglobulin protein, the specification does not teach or even suggest that VSF functions as an antibody. The data in the specification demonstrates that VSF inactivates virus via a cell-mediated immune response like a cytokine, rather than a hummoral immune response like an

immunoglobulin. This demonstrates that VSF protein is not an immunoglobulin, but a cytokine. Furthermore, it is clear from the data provided in the specification that VSF is capable of inhibiting a number of viruses, not just EMC-DV.

Therefore, the claims are sufficiently enabled and Applicants request that the rejection under 35 U.S.C. § 112, first paragraph be withdrawn.

If there are any minor issues to be resolved before a Notice of Allowance is granted, the Examiner is invited to telephone the undersigned.

Respectfully submitted,

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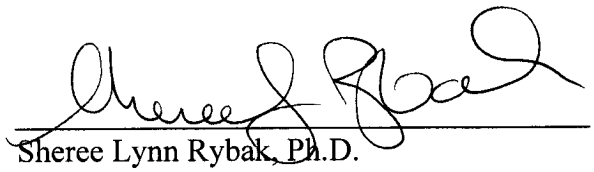
By 
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Identifying anti viral infection efficiency of VSF *in vitro* in order to screen diseases for clinical experiment

We investigated anti-iral activity of purified VSF against various viruses using modified virus inhibition test (MVIT).

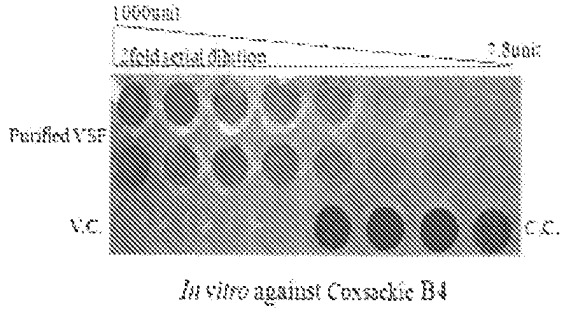

Figure: Antiviral activity of purified VSF against Coxsackie virus

The purified VSF showed partial anti-viral effect against 125 unit of Coxsackie B4 virus.